8 Adverse Events Related to Anti-D Immunoglobulin (Ig) n=418

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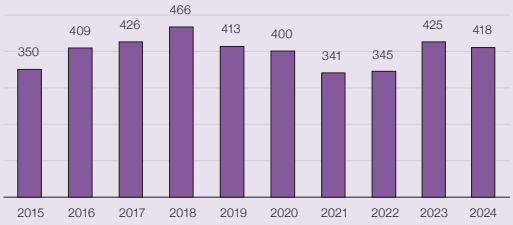
Headline data 2024

Number of reports n=418
Deaths n=0
Major morbidity n=3

Anti-D Ig reports by year



Demographic data

Male n=0
Female n=418
Adults n=409
Paediatric n=8
Unknown n=1

Potential for major morbidity n=286

Late/omitted RAADP n=91
Late/omitted anti-D Ig following a PSE (including delivery) n=195

Key findings:

- Errors related to anti-D Ig continue to account for a large proportion of SHOT cases
- The majority of errors resulted in omission or late administration. These often occur as anti-D Ig is not administered prior to discharge
- The United Kingdom and Ireland Blood Transfusion Network (UKIBTN) information leaflet Anti-D Immunoglobulin During Pregnancy, provides information to support the decision-making process

Gaps identified:

- Under-reporting of discrepancies between D-type predicted from high-throughput non-invasive prenatal testing (NIPT) for fetal *RHD* genotype and cord sample testing
- Gaps in staff knowledge about appropriate administration of anti-D Ig
- Issues with communication among staff involved in the care pathway
- Information technology (IT) issues with lack of functionality, inappropriate algorithms to support safe practice and poor interoperability

Good practice:

- Effective investigation of events and consideration of human factors enable identification of effective improvement actions
- Investigation of discrepancies between D-type predicted from cell free fetal deoxyribonucleic acid (cffDNA) screening and cord sample testing can identify wrong blood in tube (WBIT) and ensure that anti-D Ig is administered where appropriate

Next steps:

- A national comparative audit is being scheduled to identify gaps in current practice and inform improvements
- Effective use of checklists to facilitate timely administration of anti-D Ig

For all abbreviations and references used, please see the **Glossary** and **Reference list** at the end of the full Annual SHOT Report. Please see the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/annual-shot-report-2024/).

Definition:

Events relating to the requesting and/or administration of anti-D immunoglobulin (Ig) and routine antenatal anti-D Ig prophylaxis (RAADP) during pregnancy and after delivery.

Introduction

Anti-D Ig is an important aspect of management of D-negative pregnancies and in reducing the risk of developing immune anti-D in D-negative people with childbearing potential (including paediatric). This risk could also be following transfusion of D-positive blood components and D-mismatched solid organ transplants (Qureshi, et al., 2014). Guidelines for safe and appropriate administration of anti-D Ig following potentially sensitising events (PSE) and RAADP are available in the United Kingdom (UK) (Qureshi, et al., 2014; NICE, 2008; NICE, 2019; NICE, 2023). Organisations should ensure that the requirements for safe practice are reflected in local policies, systems, and processes. The SHOT aide memoire for anti-D Ig in pregnancy is based on available national guidance on the appropriate use of anti-D Ig and is freely accessible on the SHOT website.

High-throughput NIPT for fetal *RHD* genotype, i.e., cffDNA, is available across the UK for non-immunised D-negative pregnant women and birthing people, as recommended by the National Institute for Health and Care Excellence (NICE) (NICE, 2016). Prediction of the fetal D-type supports targeted administration of anti-D Ig. The screening assay has limitations, with sensitivity of 99.3% (95% confidence interval (CI) 0.982-0.997) and specificity of 98.4% (95% CI 0.964-0.993) (Mackie, et al., 2017). False-positive and false-negative results must be reported to SHOT and to the test provider. A cffDNA discrepancy investigation form is available on the SHOT website, enabling local investigation and appropriate provision of anti-D Ig.

SHOT data continue to demonstrate that errors in anti-D Ig and RAADP management occur in both clinical and laboratory settings. The management of anti-D Ig and RAADP is multifaceted; errors occur at all stages of the process, from the identification of the requirement, ordering, prescription, laboratory release, storage, and administration. In 2024, SHOT released an anti-D Ig safety notice. This provides a checklist that staff can use to measure local compliance, enabling identification of gaps and development of an action plan for improvement.

Major morbidity n=3

There were 3 cases that resulted in major morbidity (sensitisation to the D antigen). In 1 case a D-negative patient of childbearing potential received a D-positive renal transplant. Anti-D Ig was not given, and the patient developed immune anti-D.

Case 8.1: Omission of anti-D Ig administration in a D-mismatched renal transplant

A D-negative patient of childbearing potential received a D-mismatched renal transplant (D-positive donor). The renal registrar did not complete the requirement for anti-D Ig in the patient's admission booklet. Furthermore, this requirement was not identified by the renal or the surgical teams involved in the patient's care. During the incident investigation, it was stated that the transplant nurse identified the need for anti-D Ig and this was communicated to the ward staff verbally. There was no evidence of this communication in the patient's notes and no request was made to the blood transfusion laboratory. The omission of anti-D Ig was identified when anti-D was detected in the patient's plasma one-month post transplant.

The second case involved a delay in administration of anti-D Ig following an abdominal trauma at 17^{+5} weeks. No anti-D Ig was ordered initially but was given 9 days later. The woman developed immune anti-C+D which were detected at birth.

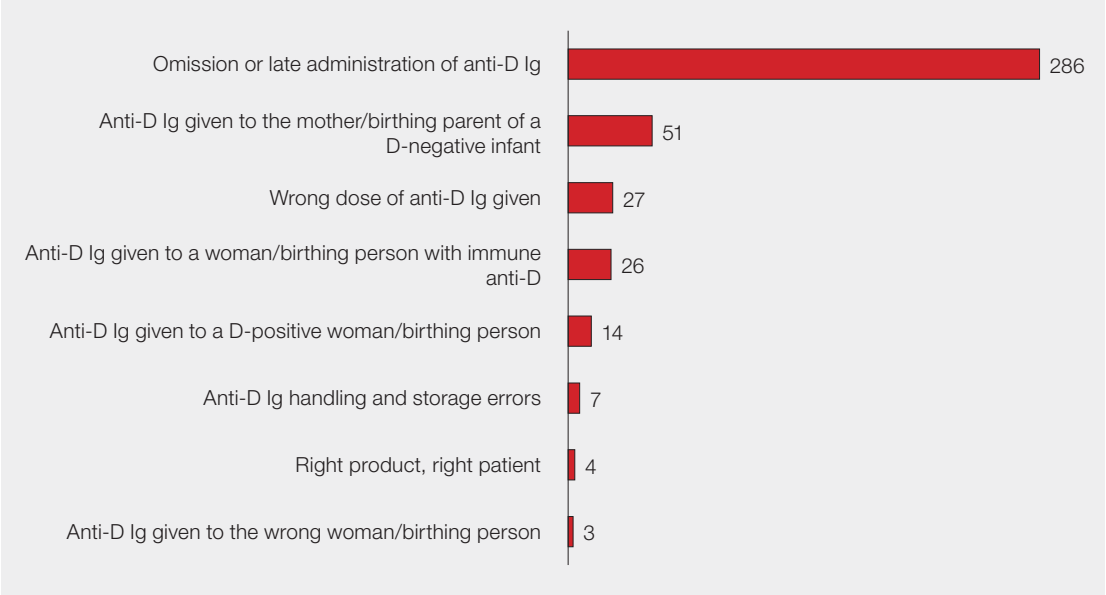
The final case occurred when follow-up testing after a large fetomaternal haemorrhage (FMH) was delayed as the sample was rejected. The sensitisation was discovered when the patient was followed up 6 months later and was found to have developed anti-D.

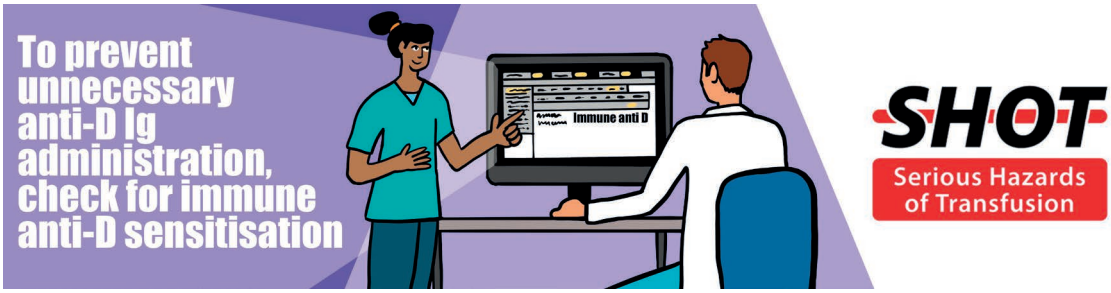
Delays, omissions, under-dosing, and failures to perform follow-up testing in a timely manner after a FMH of more than 4mL have the potential to result in development of immune anti-D and haemolytic disease of the fetus and newborn (HDFN). The impact of anti-D Ig and RAADP errors should not be underestimated.

Overview of cases n=418

A total of 418 cases have been analysed in this category, the majority of these were related to inappropriate anti-D Ig management during pregnancy. Most errors occurred in the clinical area, 330/418 (78.9%) compared to laboratory, 88/418 (21.1%). Figure 8.1 shows the distribution of cases by anti-D Ig error category.

Figure 8.1: Distribution of anti-D immunoglobulin (Ig) related error reports in 2024 (n=418)





As in previous Annual SHOT Reports the majority of errors resulted in omission or late administration of anti-D Ig, and these are further broken down in Table 8.1.

Table 8.1: Causes of omission or late administration of anti-D Ig in 2024 (n=286)

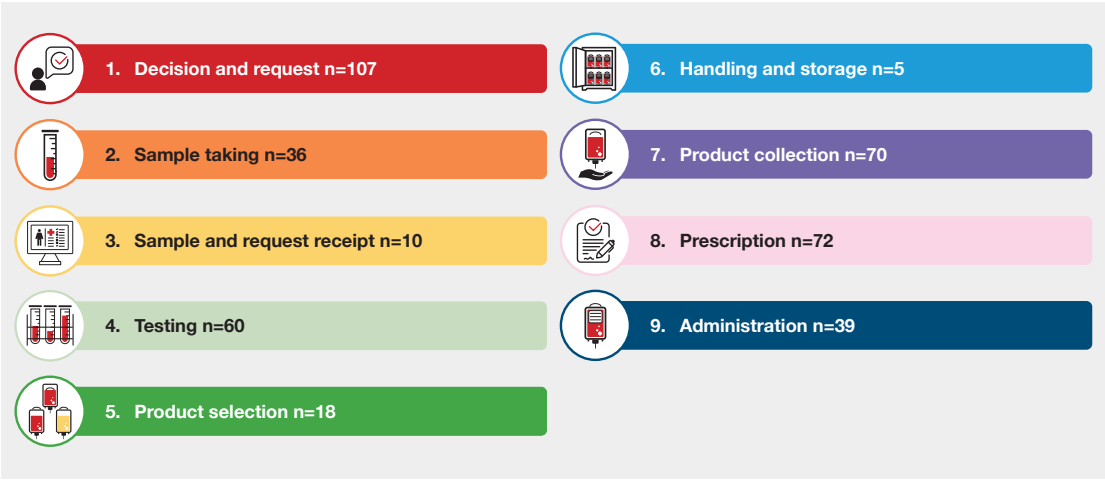
Reason for omission or late administration	Number of reports	Percentage of cases
Failure to order anti-D Ig	79	27.6%
Discharged before anti-D Ig administration	77	26.9%
Maternal or neonatal results misinterpreted or not checked	29	10.1%
Anti-D Ig ordered but not administered	26	9.1%
Incorrect decision to omit anti-D Ig administration	19	6.6%
Errors related to cffDNA testing or results	15	5.2%
Transcription errors	15	5.2%
Partial D/weak D	13	4.6%
Failure in laboratory processes	10	3.5%
Anti-D Ig errors in transplant patients	1	0.4%
Anti-D Ig stored incorrectly	1	0.4%
Failure to carry out positive patient identification	1	0.4%
Total	**286**	**100%**

From the 418 cases reported, there were 14 cases related to errors with the interpretation of D-typing results, 11 of these were partial D-type where anti-D Ig should have been given but was omitted and 3

were typed as weak D. Of the 3 cases identified as weak D, 1 was reported as D-negative and anti-D Ig given inappropriately. In 2 cases, the cord samples tested D-negative, contradictory to the D-type predicted by cffDNA screening. In 1 case, this was investigated locally and identified but anti-D Ig was not given in a timely manner, in the other case it was identified when the baby was tested in another hospital. British Society for Haematology guidelines provide an algorithm for anomalous D-typing for compatibility testing which should be reflected in local policies (Milkins, et al., 2013). No differences in error rates were seen with RAADP, 133/418 (31.8%) or with anti-D Ig given for PSE, 146/418 (34.9%) or post-birth, 139/418 (33.3%).

Anti-D Ig errors have been reported following errors at all steps in the transfusion pathway. Figure 8.2 shows the distribution of these errors. Of note, most errors occurred in clinical decision-making and requesting anti-D Ig highlighting the need for better education of staff.

Figure 8.2: Steps in the transfusion pathway when the anti-D Ig errors occurred in 2024



In 1 miscellaneous case (not included in Figure 8.1) there were two missed RAADP appointments, however it was not confirmed whether the woman had been thoroughly informed of the potential consequences of not receiving anti-D Ig in a timely manner

Information about investigation of incidents was reported in 394 cases. Of these, 295/394 (74.9%) had completed a formal investigation. Denominators for the numbers provided here is variable as this depends on whether the relevant question/s have been answered by reporters. There were 213/360 (59.2%) cases that had been discussed at a maternity governance meeting. In 96 cases, good practice was noted. The examples of good practice were varied but included individuals involved in the event being open and honest about the errors enabling effective investigations, and collaborative working to identify and implement improvement actions. Where the contribution of human factors was recorded this mainly related to:

- Failures in team function, 129/370 (34.9%)
- Gaps with staff skill or knowledge, 122/364 (33.5%)
- Inadequate written or verbal communication, 153/364 (42.0%)
- Incomplete handover, 111/394 (28.2%)

Non-invasive prenatal screening for RHD n=54

Errors related to cffDNA screening were identified in 54 cases; divided equally between laboratory (n=27) and clinical (n=27). False cffDNA results accounted for 22/27 laboratory cases, 18 false-positive cffDNA results, and 4 false-negative cffDNA negative results. The cffDNA screening test is provided by three centres in the UK, as the Welsh Blood Service introduced this test in May 2024. However, the majority of samples are tested at the International Blood Group Reference Laboratory (IBGRL). In 2024, IBGRL confirmed that there were 28 false-positive and 7 false-negative cffDNA results. This indicates an under-reporting of these events to SHOT. There was one case where the result was inconclusive and another where the cffDNA result checked was from a different pregnancy.

The main gaps identified (excluding the false-negative and false-positive cases) were related to IT where

staff did not have access to the IT system to check the result or were not trained to perform this task. Also, there were transcription errors that could have been prevented by interoperability between laboratory (reference and hospital blood transfusion laboratories) and clinical IT systems. There were also cases where the cause of error was either misinterpretation of the result or accessing results from a previous pregnancy. However, the most common cause continues to be events where cffDNA results are available but not checked prior to issuing or administration of anti-D Ig. This might reflect an ineffective process, suboptimal use of safety checks or lack of clarity in local protocols.

Investigation of cffDNA discrepancies was noted in 9 cases. The type of investigations performed in the cord samples were as follows; weak/partial D testing in 1 case, WBIT in 3 cases, WBIT and Rh (CcEe) phenotyping in 2 cases and WBIT, weak/partial D testing and Rh phenotyping together in 3 cases. It should be noted that Chapter 15a, Near Miss – Wrong Blood in Tube (WBIT) in this Annual SHOT Report describes a further 2 cases where the WBIT was identified during the investigation of discrepant cffDNA and baby's blood group results.

Further details of the cffDNA errors can be found in the supplementary chapter.

Involvement of information technology n=140

IT was noted as being involved in errors in 140/418 (33.5%) of cases (see supplementary information for details of IT issues). In 51/140 (36.4%) of these cases it was noted that IT could have prevented the error had it been in place or used. Other main contributory factors included lack of functionality/ algorithms to support safe practice, 24/140 (17.1%), lack of interfacing/interoperability, 16/140 (11.4%) and systems not being used correctly, 14/140 (10.0%).

Informed decision-making

People who are D-negative need to be informed about the benefits and risks of anti-D Ig at the earliest opportunity in pregnancy, or pre-conception. This enables them to become experts in their own health and pregnancy. Healthcare professionals have a responsibility to ensure women and birthing people have the information they need, to make informed choices about their care. It can give people the confidence and space to ask questions and establish what matters to them. Communication using plain language, reinforced with resources in their preferred format can support decision-making. The UK and Ireland Blood Transfusion Network have created a nationally agreed information leaflet about receiving anti-D Ig in pregnancy (see 'Recommended resources'). The Royal College of Midwives (RCM) provides guidance on how to support women and birthing people's informed decision-making (RCM, 2022).

Case 8.2: Delay in administering anti-D Ig

A woman was discharged from the labour ward following a vaginal bleed at 20^{+1} weeks gestation, without receiving anti-D Ig, or being advised by staff about the need for anti-D Ig. No follow up was arranged. Discharge had been recommended by the consultant overseeing the care. An FMH test had been requested but the results were not followed up by staff discharging the patient. Anti-D Ig was available after the woman was discharged. The plan of care and information given to the woman was not questioned by the midwife on duty, who was a new member of staff. The failure to administer anti-D Ig was identified by laboratory staff who checked the blood refrigerator at 72 hours. The woman was contacted by the community midwife to explain that anti-D Ig was indicated but declined to attend until the routine appointment which would have been 14 days after the PSE. Following further discussion with a haematologist, the woman agreed to come in the next day, 6 days after the PSE to receive anti-D Ig.

Knowledge gaps among staff about the need for anti-D Ig and the relevance of timing contribute to error. This case additionally highlights the importance of clear communication between all staff involved in the care pathway. Using closed loop communication, or a check-back could have ensured that the healthcare professionals accurately understood the appropriate plan of care, without assumptions being made. Open discussions and providing written information support informed and shared decision-making.

Learning points

- Working together: laboratory, gynaecology, maternity services, Trusts, Health Boards, and Integrated Care Boards should collaborate to ensure that processes and systems, including IT, are optimised to support safe practice and reduce the risk of error
- Informed decision-making: women and birthing people should be provided with the information they need to make informed choices about their care

Case 8.3: D-negative mother of D-negative baby erroneously given anti-D Ig

A woman with a predicted D-negative fetus had a PSE. Anti-D Ig was issued despite the cffDNA result being available. Following birth an order was placed in the clinical computer system for a Kleihauer, cord bloods and anti-D Ig. The system flagged a warning stating the fetus was D-negative and asking if anti-D Ig was required. The midwife on duty instructed a registered nurse caring for the woman to administer anti-D Ig. The anti-D Ig that had been issued for the antenatal PSE was used. Neither healthcare professional had noted the earlier error or heeded the warning on the IT system.

This case highlights how warning messages can be overlooked and overridden. It is not clear if the person administering the anti-D Ig had observed the system warning or had reviewed the woman's notes before administering anti-D Ig. This would have given another opportunity for the earlier error and warning message to be recognised.

The woman accepted the anti-D Ig, which underlines the importance of birthing parents and their support people understanding all aspects of their care, to enable them to make informed decisions.

Case 8.4: Unfamiliarity with managing large FMH and misinterpretation of instruction

A large FMH of 44mL was detected following birth and 1500IU anti-D Ig was given in the first instance. Upon confirmation of the FMH volume by the reference laboratory, 6500IU was advised, to be given intravenously (IV). The staff were not familiar with administering anti-D Ig IV and did not escalate this. The midwife misinterpreted the instruction to give anti-D Ig within 72 hours, as to give after 72 hours, and placed the anti-D Ig in the ward refrigerator which was not temperature controlled. The midwife documented their interpretation into the electronic patient record, and this was copied and pasted in the record across multiple shifts by other staff. The error was detected by the charge nurse after finding the anti-D Ig in the ward refrigerator, more than 72 hours after it was due to have been administered. Consultation with the reference laboratory led to a reduced dose being administered IV, after the 72-hour window had elapsed.

This case highlights the importance of a clear escalation pathway when uncommon events occur and the need for effective communication. The practice of cutting and pasting instructions in an electronic record allows incorrect decisions and misunderstanding to be perpetuated, without question. Collaboration between departments, including the laboratory and haematology staff can facilitate specialist advice as appropriate.

Near miss anti-D Ig cases n=40

There were 40 near miss cases analysed in 2024, which is similar to the numbers in 2023 (n=41). Errors were detected by laboratory staff in 8/40 (20.0%) cases, by a registered nurse or midwife in 27/40 (67.5%) and a transfusion practitioner in 3/40 (7.5%). In 2 cases, the error was detected by the woman/birthing person.

Conclusion

Errors related to anti-D Ig continue to be reported, with numbers similar to previous years despite implementation of cffDNA screening and targeted administration. SHOT has previously recommended that safe and appropriate management of anti-D Ig requires a collaborative approach with clear communication between the laboratory and other services, including maternity and gynaecology. Considering a systems approach, including application of human factors and ergonomics principles

enables implementation of barriers to error at each step in the process and enhances safety (Narayan, et al., 2024). Organisations are replacing current IT systems and implementing electronic patient record systems to better support safe practice. It is important to remember that IT systems need to be configured, maintained and used correctly to optimise benefit. Interoperability must consider all safety aspects of the system; results must file into the relevant data fields for algorithms to work without the need for additional manual transcription. IT does not replace staff knowledge, training remains key to safe practice, induction training and refresher training is critical as processes may be different across organisations.

D-negative mothers/birthing parents, or their carers, should be provided with clear information about anti-D Ig, including the risks of missing routine appointments. Every effort should be made to offer opportunities for women/birthing people to actively participate in their care. Discharge checklists should include confirmation that anti-D Ig has been administered. Reports related to anti-D Ig consistently account for a high proportion of errors reported to SHOT. SHOT provide resources to support safe practice and improvements which are all free to access on the SHOT website. Organisations are encouraged to use the available resources to build effective systems and support best practice in anti-D Ig management.

Recommended resources

SHOT Safety Notice 03: Safe, appropriate, and timely administration of anti-D Immunoglobulin during the perinatal period
https://www.shotuk.org/resources/current-resources/safety-notices/

Anti-D Immunoglobulin (Ig) Administration to avoid sensitisation in pregnancy - an aide memoire SHOT 2023
https://www.shotuk.org/resources/anti-d-immunoglobulin-ig-administration-in-pregnancy-an-aide-memoire/

The United Kingdom and Ireland Blood Transfusion Network (UKIBTN) patient information leaflet Anti-D immunoglobulin during pregnancy
https://hospital.blood.co.uk/the-update/a-new-patient-information-leaflet-anti-d-immunoglobulin-during-pregnancy/